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10/601,777	06/24/2003	Tadashi Okamoto	03560.003310.	9502

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FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
DEJONG, ERIC S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,777	OKAMOTO ET AL.	
	Examiner	Art Unit	
	Eric S. DeJong	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-24* is/are pending in the application.

4a) Of the above claim(s) *19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-18, 20,21 and 23* is/are rejected.

7)☐ Claim(s) *22 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/05/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFICE ACTION

Claim Objections

The objection of claims 1 and 20 for minor informalities is withdrawn in view of amendments made to the instant claims.

Claim Rejections - 35 USC § 112

The rejections of claims 1, 4-18 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of amendments made to the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 23 each recite the limitation "not less than 10^{10} ohm•cm (300K)" in line 2 of either of said claims. It is unclear from the instant claims what the relationship of the recited term "(300K)" to the recited range of volumetric resistivity, which renders the metes and bounds of the claim indefinite. It is acknowledged that the instant disclosure (see for example paragraphs 0034 and 0035 of the instant specification) teaches that preferably the substrate of the biochip may not be less than 10^{10} ohm•cm (300K), however this does not provide further guidance as to what the exact relationship

is between substrate temperature and the respective volumetric resistivity of a given substrate.

For the purpose of continuing examination, the limitation of "not less than 10^{10} ohm•cm (300K)" has been construed to read as a volumetric resistivity of not less than 10^{10} ohm•cm, wherein the substrate temperature is held at 300K.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Katta et al. (see second non-patent literature citation of IDS filed 01/19/2006).

The instant claims are drawn to a method and related apparatuses for acquiring information in relation to a devise comprising a substrate and a plurality of biological materials disposed on a surface of said substrate using time of flight secondary ion mass spectrometry comprising irradiating different positions on said surface in a discontinuous pattern, conducting mass-analysis of secondary ions via time of flight, and reconstructing results obtained to form two-dimensional information on the basis of said pattern.

Katta et al. set forth the methods and related apparatus for use in the accumulation of mass spectra of picomolar amounts of peptides, wherein the disclosed

apparatus irradiates a sample with a primary beam of iridium ions and the detection of mass-spectra via a secondary beam of ions generated from the irradiated sample (see Katta et al., Abstract, page 129, line 1 through page 130, line 30, and Figure 1). Further, the irradiated portion of the sample is disclosed as being smaller than the measured sample area containing the peptide sample (see Katta et al., page 138, lines 1-39).

Katta et al. further disclose that the primary ion beam is made to sweep upwards across the sample probe face, wherein secondary sample ions are emitted and detected during a short interval following the pass of the primary ion beam. In each upward sweep of the primary ion beam, sample area is irradiated a single time and not duplicated. Further, the scanning method disclosed by Katta et al. provides for a brief period during which the sample surface is not irradiated while the primary ion beam is reset to the starting position on the sample surface. As such, Katta et al. sets for a discontinuous pattern of irradiating a sample wherein irradiation of a unit area is not duplicated in one scan as instantly claimed. See Katta et al. page 133, line 2 through page 134, line 14.

Figures 9A and 9B of Katta et al. further provides for the analysis of resultant mass spectral data using two dimensional information to plot signal intensity vs. charge to mass ratio, and further compares results from experiments wherein data is acquired using the whole sample area and a single "stripe" of the sample (analyzed results on the basis of said pattern of said irradiating pulsed primary ion beam). See also Katta et al., page 142, lines 1-21).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katta et al. as applied to claims 1, 5, and 20 above, and further in view of Pellin et al.

The instant claims are drawn to a method and related apparatuses for acquiring information in relation to a devise comprising a substrate and a plurality of biological materials disposed on a surface of said substrate using time of flight secondary ion mass spectrometry comprising irradiating different positions on said surface in a discontinuous pattern, conducting mass-analysis of secondary ions via time of flight,

and reconstructing results obtained to form two-dimensional information on the basis of said pattern.

Katta et al. set forth the methods and related apparatus for use the accumulation of mass spectra of picomolar amounts of peptides, wherein the disclosed apparatus irradiates a sample with a primary beam of iridium ions and the detection of mass-spectra via a secondary beam of ions generated from the irradiated sample as discussed above. However, Katta et al. does not fairly teach or disclose that the primary ion species is a gold ion nor the use of electrically grounded substrates in combination with a reflectron type apparatus.

Pellin et al. sets forth methods and related apparatuses for applying a focused ion beam (FIB) sources that may serve as a significant improvement for Secondary Ion Mass spectrometers (SIMs). See Pellin et al., Abstract and column 1, lines 45-64.

(regarding claim 4): Pellin et al. disclose that the metal ion for the focused ion beam can be gold ions. See Pellin et al., column 3, lines 30-34 and column 6, lines 4 and 5.

(regarding claim 18): Pellin et al. further disclose a preferred embodiment of the method and system wherein the ion extracting system is grounded (see Pellin et al. column 5, lines 15-32). Further, the focused ion system disclosed by Pellin et al. is a reflection type apparatus. See for example Pellin et al., Figure 1 wherein a pulsed laser beam (14) is reflected off of a concave mirror (18) to produce metal ions.

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to modify the

apparatus and method as taught by Katta et al. to use a primary ion source of gold, a reflectron type apparatus, and to electrically ground the substrate as taught by Pellin et al. because Pellin et al. teaches these embodiments are significant improvements for Secondary Ion Mass spectrometers.

Claims 1, 5-17, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katta et al. as applied to claims 1, 5, and 20 above, and further in view of Arlinghaus et al.

The instant claims are drawn to a method and related apparatuses for acquiring information in relation to a devise comprising a substrate and a plurality of biological materials disposed on a surface of said substrate using time of flight secondary ion mass spectrometry comprising irradiating different positions on said surface in a discontinuous pattern, conducting mass-analysis of secondary ions via time of flight, and reconstructing results obtained to form two-dimensional information on the basis of said pattern.

Katta et al. set forth the methods and related apparatus for use the accumulation of mass spectra of picomolar amounts of peptides, wherein the disclosed apparatus irradiates a sample with a primary beam of iridium ions and the detection of mass-spectra via a secondary beam of ions generated from the irradiated sample as discussed above. However, Katta et al. does not fairly teach or disclose disposing samples on a chip, the use of biological materials that are a nucleic acid, DNA, RNA, PNA, or the detection of ionized components therefrom.

Arlinghaus et al. sets forth novel DNA sequencing methods that rely upon peptide nucleic acids (PNA) and hybridization biochip sensors and the use of time of flight secondary ion mass spectroscopy (TOF-SIMS) to detect short fragments thereof.

(regarding claim 6): The disclosed methodology of Arlinghaus et al. involves preparing multiple samples immobilized on silicon wafers which are further termed "biochips". See Arlinghaus et al., Title, page 951, Introduction, lines 1-20, and Experiment and Sample preparation, page 951, line 21 through page 95, line 5.

(regarding claims 7-11): Arlinghaus et al. teaches that the disclosed TOF-SIM methodology can be used in the characterization of DNA, PNA, RNA, PNA-DNA duplexes, DNA duplexes, cDNA, and the identification of expressed genes. See Arlinghaus et al., page 951, Introduction, lines 1-20.

(regarding claims 12 and 13): The spectra presented by Arlinghaus et al. in Figure 2 clearly demonstrate the masses corresponding to PO_2^- and PO_3^- of the phosphate backbone from nucleic acids.

(regarding claims 14 and 15): Arlinghaus et al. disclose in Figure 4 the signal intensity in recorded spectra related to T- and C- bases.

(regarding claims 16 and 17): Arlinghaus et al. disclose in Figure 2 the spectra resulting from TOF-SIMS analysis performed on PNA molecules that include peaks pertaining to side chains from the PNA samples immobilized on a chip surface. The side chain of the PNA molecules that are attached to the peptide backbone, which reads on the claims species derived by the ionization of amino acid residual group. See Arlinghaus et al, Figure 2 and page 952, lines 6-16.

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to rely upon the TOF-SIMS methods and apparatus of Katta et al. to investigate and detect the DNA and PNA systems as taught by Arlinghaus et al. because Katta et al. further teach that the disclosed method and systems achieve the highest possible sensitivity and make full use of the samples inserted into a mass spectrometer (see Katta et al., page 129, lines 11 and 12).

Allowable Subject Matter

Claims 21 and 23 would be allowable if rewritten to overcome the rejection under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claims 22 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

Applicant's arguments filed 06/05/2006 have been fully considered but they are not persuasive.

In regards to the rejection of claims 1, 5, and 20 under 35 U.S.C. 102(b) as being anticipated by Katta et al., applicants argue that the primary ion beam in Katta et al. is

irradiated via a conventional raster scan and the irradiated area is continuously expanded and further that raster scanning is not discontinuous.

In response, it is noted that neither the instant claims nor the instant specification provide a definition for a discontinuous scan that would exclude the embodiments from the that are taught by the prior art of record. It is further reiterated from the basis of the rejection that Katta et al. disclose that a primary ion beam is made to sweep upwards across the sample probe face, wherein secondary sample ions are emitted and detected during a short interval following the pass of the primary ion beam. In each upward sweep of the primary ion beam, sample area is irradiated a single time and not duplicated. Further, the scanning method disclosed by Katta et al. provides for a brief period during which the sample surface is not irradiated while the primary ion beam is reset to the starting position on the sample surface. As such, Katta et al. sets for a discontinuous pattern of irradiating a sample wherein irradiation of a unit area is not duplicated in one scan as instantly claimed.

In regards to the rejection of claims 1, 5-17, and 20 under 35 U.S.C. 103(a) as being unpatentable over Katta et al. in view of Arlinghaus et al. and the rejection of claims 1, 4, 5, 18 and 20 under 35 U.S.C. 103(a) as being unpatentable over Katta et al. in view of Pellin et al., applicants argue that neither Arlinghaus et al. nor Pellin et al. disclose or suggest a discontinuous scan in which there is no duplicate irradiation of the same unit area in one scan.

In response, it is noted that the instant claims do not exclude the embodiment of a discontinuous scanning method as taught by Katta et al. for the reasons provided above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

EDJ EDJ

J.S. Brusca 28 August 2006

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER